

AN 2002:868928 CAPLUS Full-text  
 DN 137:352900  
 TI Selective anthranilamide pyridine amides as inhibitors of VEGFR-2 and

VEGFR-3

IN Ernst, Alexander; Huth, Andreas; Krueger, Martin; Thierauch, Karl-Heinz;

Menrad, Andreas; Haberey, Martin

PA Schering Aktiengesellschaft, Germany

SO PCT Int. Appl., 115 pp.

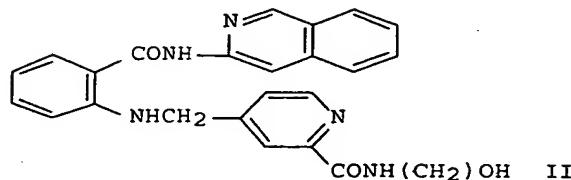
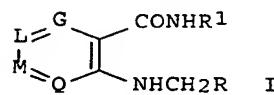
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002090352	A2	20021114	WO 2002-EP4924	20020503
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,				
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	LR, LS,				
	LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM,				
	PH, PL,				
	PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,				
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	CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
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	DE 10123574	A1	20021128	DE 2001-10123574	2001-0508
	DE 10125294	A1	20021121	DE 2001-10125294	2001-0515
PRAI	DE 2001-10123574	A	20010508		
	DE 2001-10125294	A	20010515		
	DE 2001-10164590	A	20011221		
OS	MARPAT 137:352900				
GI					



AB Title compds. I [G, L, M, Q = N, (un)substituted CH,  $\leq 1$  of them being N; R = (un)substituted N heterocycle; R1 = (un)substituted alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl] were prepared I are inhibitors of VEGFR-2 and VEGFR-3 and are used as medicaments for treating diseases that

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are caused by persistent angiogenesis, such as psoriasis, Kaposi's sarcoma, restenosis, such as e.g. stent-induced restenosis, endometriosis, Crohn's disease, Hodgkin's disease, leukemia, arthritis, such as rheumatoid arthritis, hemangioma, angiofibromatosis, in eye diseases such as diabetic retinopathy, neovascular glaucoma, in kidney diseases such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic micro-angiopathic syndrome, transplant rejection and glomerulopathy, in fibrotic diseases such as hepatic cirrhosis, mesangial-cell proliferative diseases, arteriosclerosis, damage to the nerve tissue and inhibition of the re-occlusion of vessels after balloon catheter treatment, in vessel prosthetics or after the use of mechanical devices for keeping vessels open, e.g. stents, as immunosuppressants, to support wound healing without scars and in cases of age spots and contact dermatitis. It can also be used as inhibitors of VEGFR-3 in lymphangiogenesis for hyperplastic and dysplastic changes in the lymphatic system. Thus, 2-amino-N-isoquinolin-3-ylbenzamide was treated with 2-bromo-5-pyridinecarboxaldehyde, followed by carboxylation and amidation to give the amide II. II had IC<sub>50</sub> for inhibition of VEGFR-2 of 40 nM and for inhibition of cytochrome 450 isoenzyme 2C9 of 2.9 μM.

IT 474798-53-3P 474798-54-4P 474798-55-5P  
 474798-56-6P 474798-57-7P 474798-58-8P  
 474798-59-9P 474798-60-2P 474798-61-3P  
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 474798-89-5P 474798-90-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

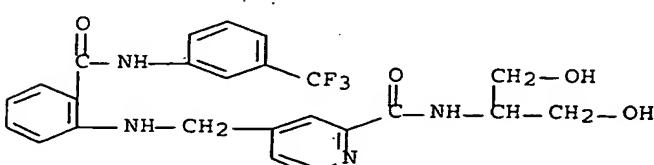
(preparation of

isoquinolinylcarbamoylphenylaminomethylpyridinecarboxamides as VEGFR-2 and VEGFR-3 inhibitors)

RN 474798-53-3 CAPLUS

CN 2-Pyridinecarboxamide, N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA

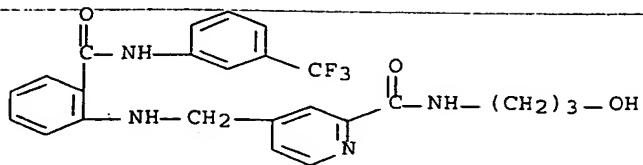
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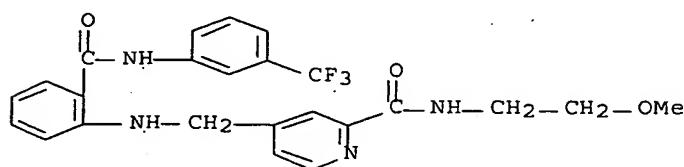
CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-4-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA

INDEX NAME)



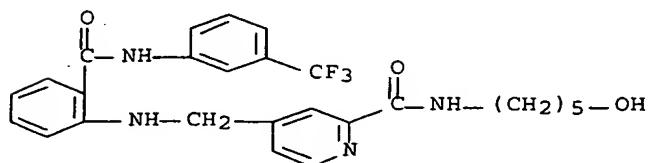
RN 474798-55-5 CAPLUS

CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



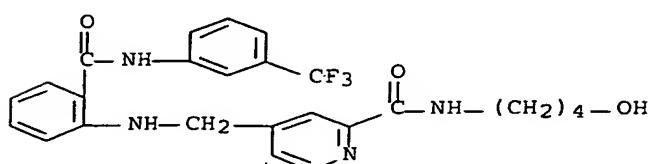
RN 474798-56-6 CAPLUS

CN 2-Pyridinecarboxamide, N-(5-hydroxypentyl)-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



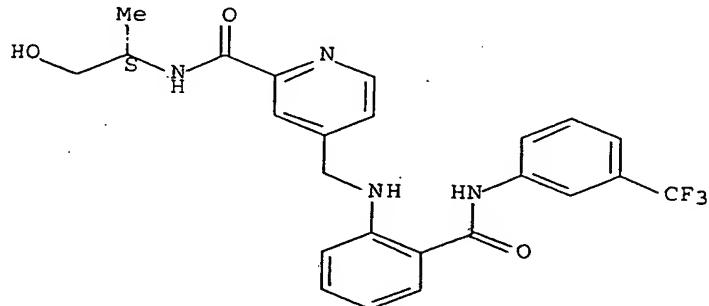
RN 474798-57-7 CAPLUS

CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



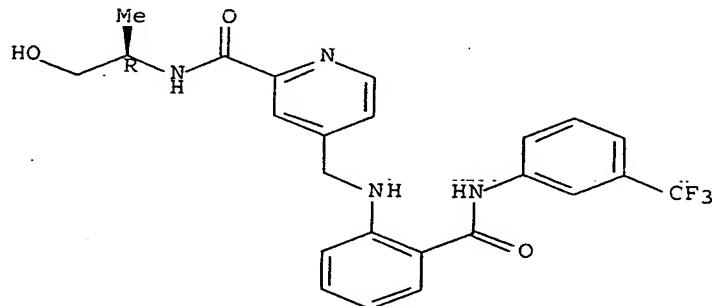
RN 474798-58-8 CAPLUS  
CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-4-[[[2-  
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- (trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



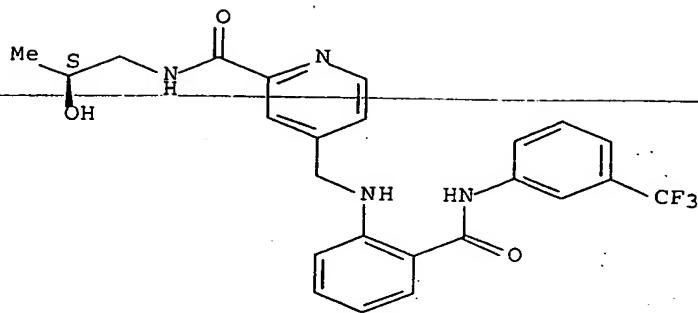
RN 474798-59-9 CAPLUS  
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-4-[[[2-  
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- (trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



RN 474798-60-2 CAPLUS  
CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-4-[[[2-[[3-  
- (trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

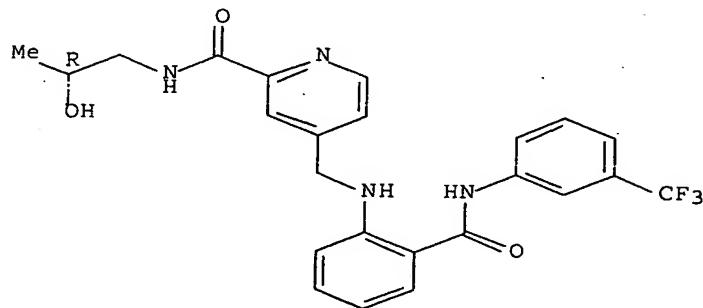
Absolute stereochemistry.



RN 474798-61-3 CAPLUS

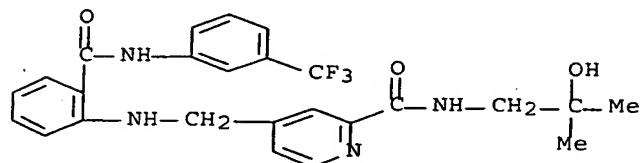
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



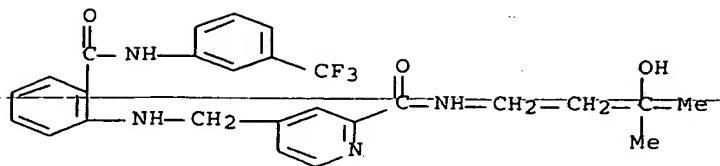
RN 474798-62-4 CAPLUS

CN 2-Pyridinecarboxamide, N-(2-hydroxy-2-methylpropyl)-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



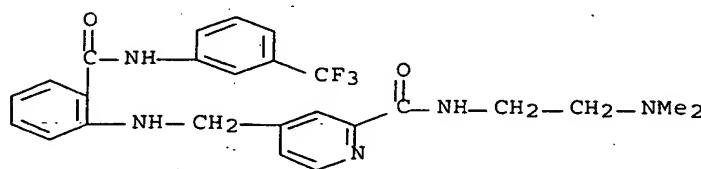
RN 474798-63-5 CAPLUS

CN 2-Pyridinecarboxamide, N-(3-hydroxy-3-methylbutyl)-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



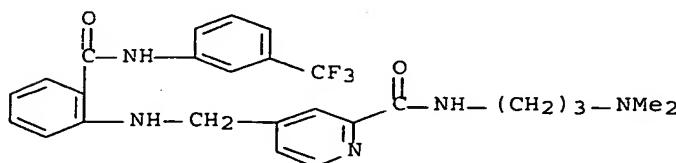
RN 474798-64-6 CAPLUS

CN 2-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



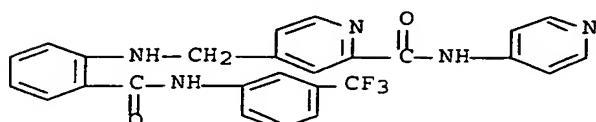
RN 474798-65-7 CAPLUS

CN 2-Pyridinecarboxamide, N-[3-(dimethylamino)propyl]-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



RN 474798-66-8 CAPLUS

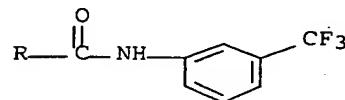
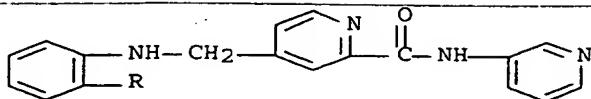
CN 2-Pyridinecarboxamide, N-4-pyridinyl-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



RN 474798-67-9 CAPLUS

CN 2-Pyridinecarboxamide, N-3-pyridinyl-4-[[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA

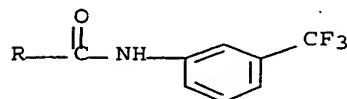
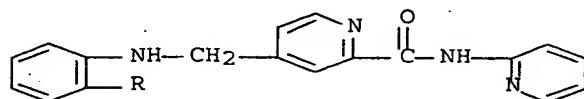
INDEX NAME)



RN 474798-68-0 CAPLUS

CN 2-Pyridinecarboxamide, N-2-pyridinyl-4-[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA

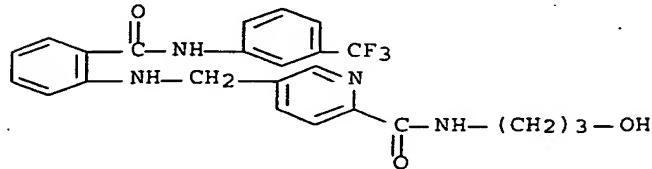
INDEX NAME)



RN 474798-75-9 CAPLUS

CN 2-Pyridinecarboxamide, N-(3-hydroxypropyl)-5-[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA

INDEX NAME)

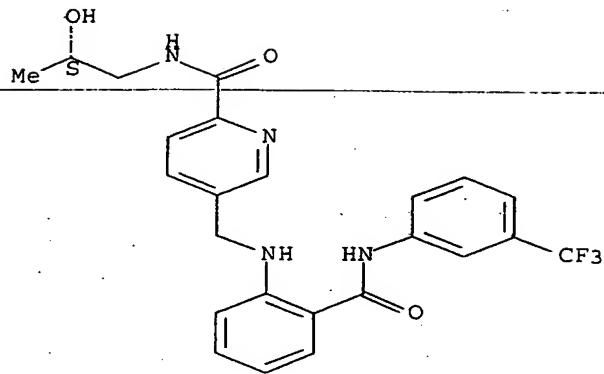


RN 474798-76-0 CAPLUS

CN 2-Pyridinecarboxamide, N-[(2S)-2-hydroxypropyl]-5-[[2-[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA

INDEX NAME)

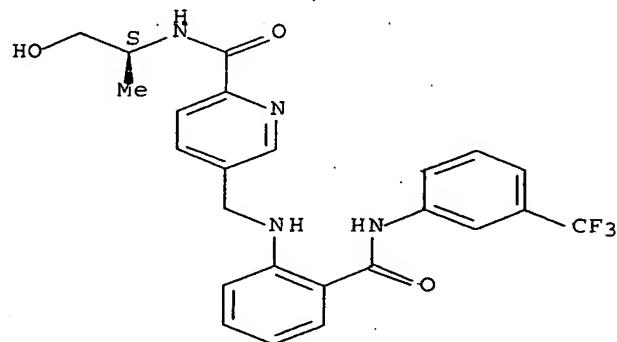
Absolute stereochemistry.



RN 474798-77-1 CAPLUS

CN 2-Pyridinecarboxamide, N-[(1S)-2-hydroxy-1-methylethyl]-5-[[[2-  
[[3-  
    (trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

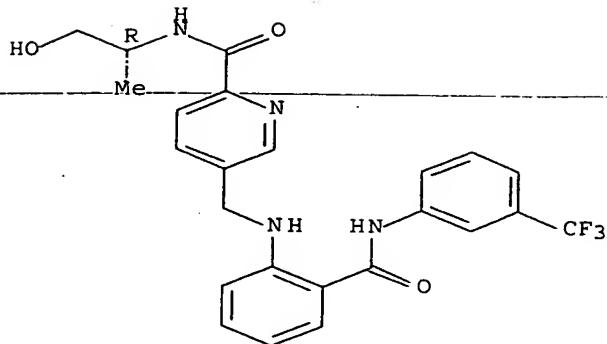
Absolute stereochemistry.



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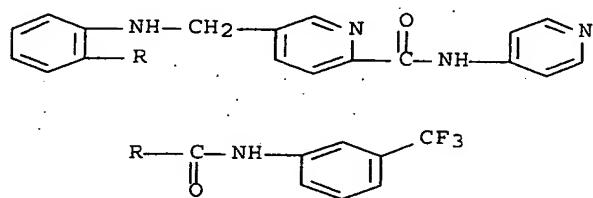
CN 2-Pyridinecarboxamide, N-[(1R)-2-hydroxy-1-methylethyl]-5-[[[2-  
[[3-  
    (trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



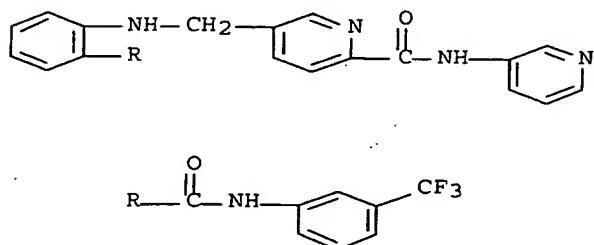
RN 474798-79-3 CAPLUS

CN 2-Pyridinecarboxamide, N-4-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



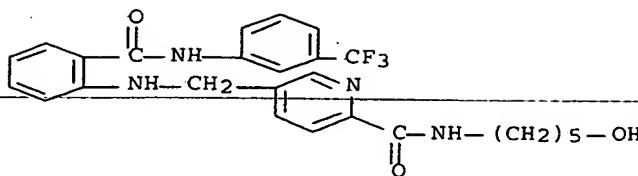
RN 474798-80-6 CAPLUS

CN 2-Pyridinecarboxamide, N-3-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



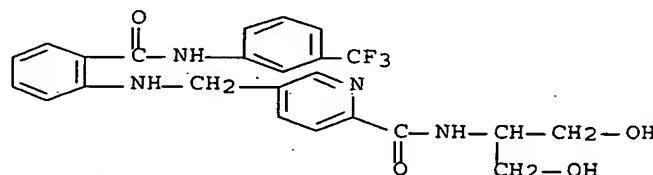
RN 474798-81-7 CAPLUS

CN 2-Pyridinecarboxamide, N-(5-hydroxypentyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA INDEX NAME)



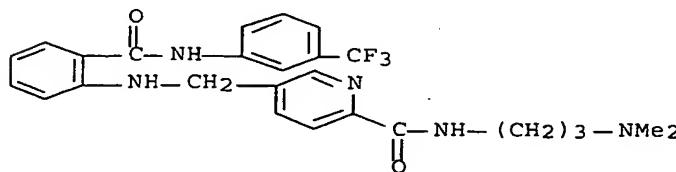
RN 474798-82-8 CAPLUS

CN 2-Pyridinecarboxamide, N-[2-hydroxy-1-(hydroxymethyl)ethyl]-5-[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



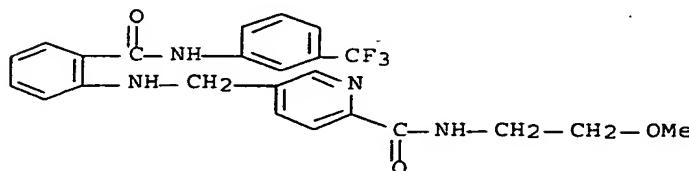
RN 474798-83-9 CAPLUS

CN 2-Pyridinecarboxamide, N-[3-(dimethylamino)propyl]-5-[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



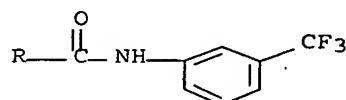
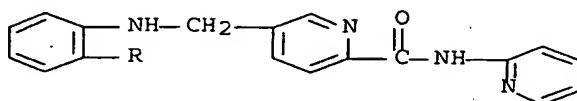
RN 474798-84-0 CAPLUS

CN 2-Pyridinecarboxamide, N-(2-methoxyethyl)-5-[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

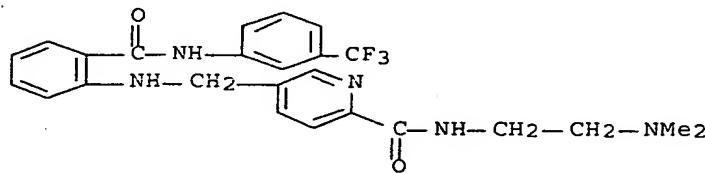


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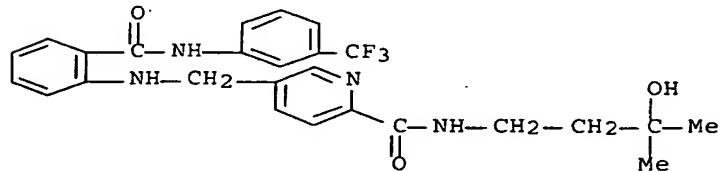
CN 2-Pyridinecarboxamide, N-2-pyridinyl-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA  
INDEX NAME)



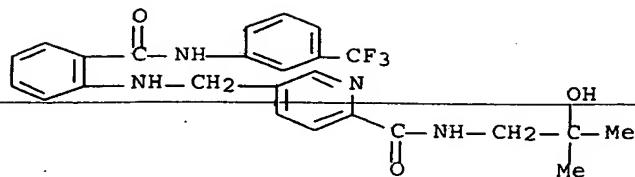
RN 474798-86-2 CAPLUS  
CN 2-Pyridinecarboxamide, N-[2-(dimethylamino)ethyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA  
INDEX NAME)



RN 474798-87-3 CAPLUS  
CN 2-Pyridinecarboxamide, N-(3-hydroxy-3-methylbutyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA  
INDEX NAME)



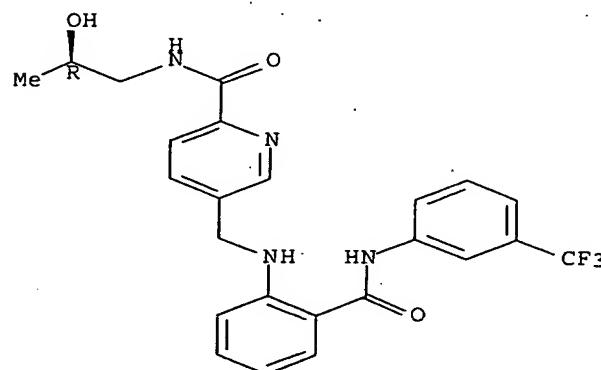
RN 474798-88-4 CAPLUS  
CN 2-Pyridinecarboxamide, N-(2-hydroxy-2-methylpropyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-(9CI) (CA  
INDEX NAME)



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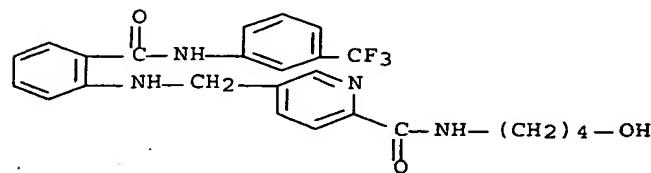
CN 2-Pyridinecarboxamide, N-[(2R)-2-hydroxypropyl]-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



RN 474798-90-8 CAPLUS

CN 2-Pyridinecarboxamide, N-(4-hydroxybutyl)-5-[[[2-[[[3-(trifluoromethyl)phenyl]amino]carbonyl]phenyl]amino]methyl]-  
(9CI) (CA  
INDEX NAME)



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